Correlation of endometrial thickness, cycle day and histopathology in women with abnormal uterine bleeding

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ABSTRACT

Objective: To correlate the endometrial thickness measured by transvaginal sonography (TVS), cycle day and menstrual status with histopathology in women with abnormal uterine bleeding and to evaluate the accuracy of transvaginal sonography in detecting intrauterine abnormalities as compared to hysteroscopy.

Methods: This prospective study was conducted in the Department of Obstetrics and Gynecology, Sultan Qaboos University Hospital between January 1998 and July 2002. Transvaginal sonography was performed in 160 women with abnormal uterine bleeding, followed within 48 hours by hysteroscopy and endometrial biopsy. Statistical analysis was performed by MacNamar's chi-square test and the various correlations were calculated.

Results: No statistically significant association was found between endometrial thickness and cycle day with histopathology. None of the women with endometrial thickness of <5 mm had atypia or malignancy. There was a highly significant association between menstrual status and histology. Transvaginal sonography and hysteroscopy were in agreement in 73.7% of the patients.

Conclusion: An endometrial thickness of <5 mm in women with postmenopausal bleeding could mean that curettage can be avoided. No definite cut-off value could be assigned for the menstruating women. Transvaginal sonography is a good initial screening tool in the evaluation of women with abnormal uterine bleeding. Hysteroscopy and histological examination is indicated in cases of abnormal or inconclusive sonograms or if complaints persist after a normal sonogram. Transvaginal sonography seems to be an effective procedure to exclude endometrial and intrauterine abnormalities.

Saudi Med J 2005; Vol. 26 (2): 260-263

Up to 33% of women referred to gynecology out-patient clinics have abnormal uterine bleeding and this incidence rises to 69% in a peri or postmenopausal group.[1,2] Endometrial curettage alone was considered to be essential in the management of perimenopausal and postmenopausal bleeding. The accuracy and effectiveness of this procedure is questionable. The false negative rate ranges from 2–6%.[1,3,4] Grimes[1] reported that the adequacy of specimens collected for histologic interpretation varies from 77–94%. The acceptance of the use of transvaginal sonography (TVS) for the evaluation of normal and abnormal endometrium is increasing. Fleischer et al[5] showed a good correlation between TVS and endometrial histology in menstruating and postmenopausal patients. In recent years, diagnostic hysteroscopy has proved to be a reliable method of evaluating intrauterine abnormalities.[3,5,6] A review of literature shows only a few studies combining the endometrial thickness, cycle day, hysteroscopy findings and histology. We undertook this study to correlate endometrial thickness, cycle day and

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Received 26th June 2004. Accepted for publication in final form 18th September 2004.

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menstrual status with hysteroscopy findings and histology in women with abnormal uterine bleeding and to evaluate the accuracy of TVS in detecting intrauterine abnormalities as compared to hysteroscopy.

Methods. This was a prospective study conducted in the Department of Obstetrics and Gynecology, Sultan Qaboos University Hospital between January 1998 and July 2002. One hundred and sixty women with abnormal uterine bleeding were included in the study. Informed consent was taken from all the patients. Patients were divided into 3 groups – menstruating, perimenopausal (>45 years till menopause) and menopausal. Age, parity and presenting symptoms were recorded.

Transvaginal sonography was performed using a Toshiba Sonolayer HX 2061-0101 and a vaginal probe of 7.5 MHz. Endometrial thickness was measured at the thickest part in the longitudinal plane and included both endometrial layers from one basalis to the contralateral basalis including the uterine cavity. The cycle day on which the sonography was performed was recorded along with any other detected uterine abnormality. Hysteroscopy and endometrial curettage was scheduled within 24 – 48 hours of the TVS as an in-patient procedure under general anesthesia. A 5 mm continuous flow rigid Olympus hysteroscope (Olympus Optical Co. Europe GmbH, Hamburg, Germany) with Ringer Lactate as the distension medium was used. The findings of TVS and hysteroscopy were compared. Histology of the curetted endometrium was also recorded.

Results. A total of 160 patients completed the study. The distribution of patients according to their age and parity is shown in **Table 1**. The age ranged from 25-85 years. Menorrhagia was the most common presenting symptom in 99 women (62%), followed by metrorrhagia in 35 women (22%). Twenty-six women (16%) were postmenopausal. The correlation between endometrial thickness and histology is shown in **Table 2.** Patients were divided into 5 groups based on endometrial thickness and histopathology. Seventy-one women had a proliferative endometrium followed by secretory endometrium in 40 women. Out of 27 women with hyperplastic endometrium, only 3 showed atypia (endometrial thickness 16-20 mm). Twenty-three women had simple hyperplasia and 4 had complex hyperplasia. The group classified as "others" includes metaplasia, endometrial polyps and hormonal effects. The endometrial thickness ranged from 2.5-22.5 mm. The mean endometrial thickness in the 3 groups were as follows: menstruating – 11.5 mm (range 3 – 29 mm), perimenopausal – 10.7 mm (range 4 – 22.4 mm) and postmenopausal – 10 mm (range 2.5 – 20 mm). **Table 3** shows the pattern of endometrial histology according to cycle day. Thirty-six women were examined in the first half of the menstrual cycle and 34 of them had proliferative endometrium. Forty-seven women were examined in the second half of the cycle and 17 of them had proliferative endometrium. Sixteen women had prolonged cycles and 26 were postmenopausal. In all the groups, proliferative endometrium was the most common histological pattern.

The endometrial histology seen in menstruating, perimenopausal and postmenopausal women is shown in **Table 4**. Most of our patients (99), were in the menstruating group. Transvaginal sonography and hysteroscopy findings were in agreement in 118 cases (73.8%). Of these, 88 women had normal hysteroscopy and TVS findings and 30 women had abnormal findings on both TVS and hysteroscopy. In the remaining 42 women, hysteroscopy and TVS findings did not correlate. Twenty-six women with normal TVS had some endometrial abnormalities detected by hysteroscopy. Sixteen patients with abnormal TVS did not have any abnormality on hysteroscopy, probably due to thickened endometrium being mistaken for a polyp or fibroid. The sensitivity of TVS in the detection of

Table 1 - Age and parity profile.

Age (years)	Nulli para	Parity 1-5	Parity >5	Total
21-30	5	4	1	10
31-40	7	25	19	51
41-50	4	32	37	73
51-60	0	14	7	21
>61	1	3	1	5
Total	**17**	**78**	**65**	**160**

Table 2 - Correlation between endometrial thickness and histology.

Histology	Endometrial Thickness millimeters <5	5-10	11-15	16-20	>20	Total
Proliferative	5	34	27	5	0	**71**
Secretory	0	21	14	3	2	**40**
Hyperplastic	0	0	10	9	8	**27**
Atrophic	8	0	0	0	0	**8**
Others	1	3	8	2	0	**14**
Total	**14**	**58**	**59**	**19**	**10**	**160**

endometrial abnormalities was 53.6% whereas the specificity was 84.6%.

Discussion. Abnormal uterine bleeding is a common problem accounting for more than 70% of all gynecological consultations in the peri- and postmenopausal years.[7] The main aim of investigating these women was to rule out endometrial cancer and its precursor lesion and endometrial hyperplasia. The probability of endometrial cancer in women presenting with postmenopausal bleeding is 10% and approximately 15% for endometrial hyperplasia.[8] The prevalence of benign intrauterine structural pathology (example, endometrial polyps and intracavitary fibroids) found in association with bleeding was 25%.[8,9]

For many years, diagnostic curettage has been the method of choice to diagnose endometrial abnormalities.[1] Hysteroscopy combined with histologic examination subsequently became the "gold standard" for such evaluation.[6,10] In recent years, the focus has shifted to TVS as a simple, non-invasive alternative method to hysteroscopy and curettage.[3] The advent of high resolution transvaginal probes have revolutionized the ability to visualize the endometrium. Transvaginal sonography is an accurate instrument for the evaluation of the endometrium in menstruating as well as postmenopausal women.[3,6,11]

In the Nordic Trial, where over 1100 postmenopausal women were evaluated, it was found that for a cut-off value of endometrial thickness of 4 mm, the sensitivity was 96% and specificity was 68% to detect endometrial abnormalities (polyp, hyperplasia, carcinoma). If a cut-off of 5 mm was used, the specificity increased but 2 carcinomas were missed.[12]

In menstruating women, the endometrial thickness increases gradually and measures 10-12 mm by the day of ovulation and increases further up to 16 mm by the mid-luteal phase.[6] However, there is a lack of clear cut-off criteria for abnormal endometrial thickness for pre-menopausal women. In the present study of 160 women with abnormal uterine bleeding ranging in age from 25-85 years, we did not find any statistically significant correlation between endometrial thickness and histopathology, but none of the patients with endometrial thickness <5 mm had atypia. There was no significant association between cycle day and abnormal histology. A highly significant association between menstrual status and histopathology was found in our study as expected. On reviewing the literature, we could not find any study comparing cycle day and menstrual status with histopathology. Abnormal sonograms were defined by us as sonograms showing fibroids or polyps projecting into the uterine cavity. Among 114 women with normal sonograms, small endometrial polyps were not visualized in 26 women. These polyps were probably masked by a very hyper echo-dense late secretory endometrium. Transvaginal sonography in the proliferative phase of the cycle could eliminate these false negative findings.[13] The sensitivity of TVS can be improved greatly by saline infusion sonography.[14] The percentage of abnormal findings detected by hysteroscopy was 35% and 28.7% for TVS. This difference is statistically significant ($p<0.05$). The results demonstrate the superiority of hysteroscopy over TVS for the exclusion of intrauterine abnormalities in women with abnormal uterine bleeding.

An endometrial thickness of <5 mm in women with postmenopausal bleeding could mean that curettage could be avoided. No definite cut-off value can be assigned for the menstruating women. Transvaginal sonography is a good initial screening tool in the evaluation of women with abnormal uterine bleeding. Hysteroscopy and histological examination is indicated in cases of abnormal or inconclusive sonograms or if complaints persist

Table 4 - Endometrial histology in the various menstrual groups.

Histology	Menstrual (<45 yrs)	Perimenopausal (45 yrs menopause)	Post menopausal	Total
Proliferative	48	18	5	**71**
Secretory	29	11	0	**40**
Hyperplastic	17	5	5	**27**
Atrophic	0	0	8	**8**
Others	5	1	8	**14**
Total	**99**	**35**	**26**	**160**

Table 3 - Correlation between histology and cycle day (patients with metrorrhagia excluded).

Histology	Cycle day			Post menopausal	Total
	< 14	15-30	> 30		
Proliferative	34	17	11	5	**67**
Secretory	0	20	3	0	**23**
Hyperplastic	0	9	1	5	**15**
Atrophic	0	0	0	8	**8**
Others	2	1	1	8	**12**
Total	**36**	**47**	**16**	**26**	**125**

after a normal sonogram. Transvaginal sonography seems to be an effective procedure to exclude endometrial and intrauterine abnormalities.

Acknowledgment. We thank Dr. Syed G. Rizvi, Assistant Professor, Department of Epidemiology and Statistics for his valuable help in the statistical analysis of the data.

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